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Abstract

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Free-Radical Addition of N-Alkylacetamides to Methyl Acrylate

Aliphatic amines add to α-olefins in the presence of tert-butyl peroxide with formation of products of α-C-alkylation ([1]). The radical addition reaction of acylated methylamine—N-methylacetamide—to α-olefins proceeds at the CH_3 group attached to nitrogen, yielding the corresponding N-alkylacetamide. At a molar ratio of N-methylacetamide : octene-1 : tert-butyl peroxide of $3 : 1 : 0.06$, a temperature of 128°, and an experiment duration of 42 hours, the yield of N-nonylacetamide was 33% ([2]).

In the present communication we give the results of a study of the reaction of certain N-alkylacetamides with methyl acrylate. Our task was to develop a new route for the synthesis of γ-amino acids and, from the latter, the corresponding pyrrolidones-2.

It was established that, when the reaction is initiated by tert-butyl peroxide, N-alkylacetamides add to methyl acrylate with formation of methyl esters of γ-N-acetylamino acids according to the following scheme:

$$R{-}CH_2NHCOCH_3 + CH_2{=}CH{-}COOCH_3 \rightarrow R{-}\underset{\displaystyle NHCOCH_3}{\underset{|}{CH}}{-}CH_2CH_2COOCH_3$$

The conditions of individual experiments are given in Table 1. The reaction of N-methylacetamide, which is a poor chain-transfer agent, with methyl acrylate leads to formation of a $1 : 1$ adduct in low yield; mainly telomerization products are formed here. Acylated ethylamine, butylamine, and piperidine transfer the chain considerably better than N-methylacetamide; therefore, even when a smaller amount of peroxide is used, the yield of $1 : 1$ adducts in experiments II-IV is 60–70%. For a comparative evaluation of the reactivity of methyl acrylate and other unsaturated compounds in the reaction with acylated amines, two experiments (V and VI) were carried out,

Table 1

Reaction of N-alkylacetamides (A) with unsaturated compounds (B)

Experiments No.	Reaction components A	Reaction components B	Amounts taken into reaction, mol A	Amounts taken into reaction, mol B	Amounts taken into reaction, mol peroxide	Temperature, °C	Duration, hours	Yield of 1 : 1 adduct, g	Yield of 1 : 1 adduct, %	Residue, g
I	$CH_3NHCOCH_3$	$CH_2{=}CHCOOCH_3$	0.3	0.3	0.075	155–160	6	15.3	32	26
II	$C_2H_5NHCOCH_3$	$CH_2{=}CHCOOCH_3$	0.3	0.3	0.03	155–160	6	36.5	70	13
III	$C_4H_9NHCOCH_3$	$CH_2{=}CHCOOCH_3$	0.2	0.3	0.02	155–160	6	24	60	12
IV	$(CH_2)_5NCOCH_3$	$CH_2{=}CHCOOCH_3$	0.3	0.3	0.015	155–160	6	20	62	10
V	$(CH_2)_5NCOCH_3$	$CH_2{=}CHC_6H_{13}$	0.3	0.3	0.013	155–160	6	6.5	21	11.5
VIa	$C_4H_9NHCOCH_3$	$CH_2{=}CH(CH_2)_2COOCH_3$	0.16	0.16	0.0375	155–160	6	12	35	19
VI	$C_4H_9NHCOCH_3$	$CH_2{=}CH(CH_2)_2COOCH_3$	0.14	0.14	0.014	155–160	6	9.6	30	11.5

in which the unsaturated components were octene-1 and allylacetic acid. From the data in Table 1 it is seen that the yields of the 1 : 1 adduct with an α-olefin (experiments IV, V) and with the ester of allylacetic acid (experiments III, VI) are 2–3 times lower than with methyl acrylate. These results may be explained by the fact that the delocalization energy of the intermediate carbomethoxy-conjugated radical $R\text{—}NH(COCH_3)CH_2\text{—}\dot{C}HCOOCH_3$ (A′) is higher than the energy of the radicals $RNH(COCH_3)CH_2\dot{C}HC_6H_{13}$ (B′) and $RNH(COCH_3)CH_2\text{—}\dot{C}HCH_2CH_2COOCH_3$ (B′); chain transfer by radical A′ also proceeds more readily than by radicals B′ and B′.

From the adducts of methyl acrylate with N-acetylbutylamine and N-acetylpiperidine, 5-propyl-2-pyrrolidone and 1,5-tetramethylene-2-pyrrolidone (3-oxaoctahydroindolizine), respectively, were obtained by the usual procedure.

$$\text{N-acetylpiperidine} + CH_2{=}CH\cdot COOCH_3 \longrightarrow \text{N-acetylpiperidine-}CH_2CH_2COOCH_3 \xrightarrow[2.\ HCl]{1.\ KOH}$$

$$\longrightarrow \text{piperidinium-}CH_2CH_2COOH\cdot HCl \xrightarrow{KOH} \text{1,5-tetramethylene-2-pyrrolidone}$$

Experimental Part

Experiment 1. Methyl ester of N-acetyl-γ-aminobutyric acid. To 198 g (2.7 mol) of N-methylacetamide at 155–160° over 6 h, a solution of 25.8 g (0.3 mol) of methyl acrylate and 11 g (0.075 mol) of tert-butyl peroxide in 22 g (0.3 mol) of N-methylacetamide was added uniformly, after which the reaction mixture was heated for one more hour at 155–160°. By vacuum distillation of the reaction mixture there were isolated the decomposition products of the peroxide, 202 g of the initial N-methylacetamide, and 15.3 g of methyl ester of N-acetyl-γ-aminobutyric acid with b.p. 117–118° (1 mm), n_D^{20} 1.4582, d_4^{20} 1.0893; MR found 39.89; calculated 39.91.

Found, %: C 52.95, 53.01; H 8.23, 8.27
$C_7H_{13}NO_3$. Calculated, %: C 52.81; H 8.23

High-boiling residue—26 g. Experiments II–VI were carried out by the previously described procedure.

Experiment II. Methyl ester of N-acetyl-γ-aminovaleric acid. B.p. 108–109° (0.5 mm), n_D^{20} 1.4582; d_4^{20} 1.0564; MR found 44.54; calculated 44.56.

Found, %: C 55.32, 55.32; H 8.86, 8.75
$C_8H_{15}NO_3$. Calculated, %: C 55.47; H 8.72

Experiment III. Methyl ester of N-acetyl-γ-aminoenanthic acid. B.p. 122.5–125° (0.5 mm), m.p. 52–53° (after recrystallization from hexane).

Found, %: C 59.45, 59.70; H 9.36, 9.47
$C_{10}H_{19}NO_3$. Calculated, %: C 59.67; H 9.51

Hydrochloride of γ-aminoenanthic acid. A mixture of 5 g of the ester of N-acetyl-γ-aminoenanthic acid, 8.5 g of KOH, and 19 g of water was boiled for 7 h, after which an excess amount of concentrated hydrochloric acid was added to the mixture, the solution was evaporated to dryness, and the residue was extracted with absolute ethyl alcohol. The alcoholic solution was evaporated and treated with absolute ether; the precipitated crystals of γ-aminoenanthic acid hydrochloride (3.6 g; yield 80%) were filtered off, m.p. 96–97° C.

5-Propyl-2-pyrrolidone. A mixture consisting of 18.1 g of the ester of N-acetyl-γ-aminoenanthic acid, 30.4 g of KOH, and 71 g of water was boiled for 7 h, neutralized with the calculated amount of hydrochloric acid, and evaporated to dryness. To the salt formed, 200 ml of nonane was added, after which the reaction mixture was boiled for 6 h. From the nonane solution, distillation gave 6.9 g (60% yield) of 5-propyl-2-pyrrolidone, mp 55–56° (from octane).

Found, %: C 66.08, 65.98; H 10.41, 10.20
$C_7H_{13}NO$. Calculated, %: C 66.10; H 10.30

Experiment IV. Methyl ester of β-(N-acetyl-2-piperidyl)propionic acid. Bp 112–113° (0.5 mm), n_D^{20} 1.4848; d_4^{20} 1.0923; MR found 56.44;

calculated 56.36.

Found, %: C 61.94, 61.81; H 9.10, 8.91
$C_{11}H_{19}NO_3$. Calculated, %: C 61.39; H 8.89

Hydrochloride of β-(2′-piperidyl)propionic acid. Obtained in 82% yield, mp 157–158°C.

1,5-Tetramethylene-2-pyrrolidone. It was obtained by gradual addition of a 30% KOH solution to the hydrochloride of β-(2′-piperidyl)propionic acid. The organic layer formed was separated from the aqueous layer and distilled. Yield of 1,5-tetramethylene-2-pyrrolidone 90%, bp 73° (0.5 mm), n_D^{20} 1.5031; d_4^{20} 1.0648; MR found 38.89; calculated 38.65.

Found, %: C 68.68, 68.55; H 9.54, 9.62
$C_8H_{13}NO$. Calculated, %: C 69.02; H 9.41

Experiment V. N-Acetyl-α-octylpiperidine. Bp 117-118° (0.5 mm); n_D^{20} 1.4754; d_4^{20} 0.9254; MR found 72.90; calculated 73.48.

Found, %: C 75.19; 75.24; H 12.08, 12.30
$C_{15}H_{29}NO$. Calculated, %: C 75.25; H 12.21

Experiment VI. Methyl ester of N-acetyl-ϵ-aminocapric acid. Bp 159-163° (1 mm), mp from benzene–octane solution 85–86°.

Found, %: C 62.55, 62.68; H 10.05, 10.08
$C_{12}H_{23}NO_3$. Calculated, %: C 62.85; H 10.10

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References Cited

1. W. H. Ury, O. O. Juveland, *J. Am. Chem. Soc.*, **80**, 3322 (1958).

2. F. Friedman, H. Shechter, *Tetrahedron Letters*, No. 7, 238 (1961).

Note: Figure translations are in progress. See original paper for figures.